Beispiel 4:

Augentropen mit 0,05 % Azelastinhydrochlorid.

140 g Polyvinylalkohol (Handelsname zum Beispiel: Mowiol 26 - 88 / Hoechst AG, Frankfurt 80) werden in 4 Liter kaltes Wasser für Injektionszwecke eingerührt, die Suspension auf 90°C erwärmt und 45 Minuten bei dieser Temperatur belassen. Die erhaltene Lösung wird mit folgenden Lösungen gemischt: 5 g Azelastinhydrochlorid in 1 Liter Wasser für Injektionszwecke, 0,2 g Phenylquecksilbernitrat in 2 Liter Wasser für Injektionszwecke, 70 g Natriumchlorid in 1 Liter Wasser für Injektionszwecke.

Die Mischung wird durch Zusatz von 0,1 N Natronlauge für einen pH-Wert von 6,8 eingestellt, mit einer Lösung von 15 g Natriumdihydrogenphosphat.2 H_2O und 21 g Dinatriumhydrogenphosphat.2 H_2O in 1 Liter Wasser für Injektionszwecke vermischt und mit Wasser für Injektionszwecke auf 10 Liter aufgefüllt.

Nach sorgfältigem Mischen wird die Lösung durch ein Membranfilter der Porenweite 0,2 µm mit Glasfaservorfilter filtriert und nach Verwerfen eines Vorlaufs von 500 ml unter aseptischen Bedingungen in sterile Augentropfenflaschen abgefüllt.

Azelastin enthaltende Arzneimittel zur Anwendung in der Nase und/oder am Auge

Zusammenfassung:

Arzneimittel zur nasalen Anwendung oder zur Anwendung am Auge, welches als Wirkstoff Azelastin enthält, wobei das Azelastin auch in Form eines physiologisch verträglichen Salzes vorliegen kann.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

WM.

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/268,772	11/09/88	HETTCHE H	699187217PH

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036

EXAMINER	
PRATER, F	
ART UNIT	PAPER NUMBER
158	2

06/23/89

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-18 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-18 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☑ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☑ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

MP0050

EXAMINER'S ACTION

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-18 are rejected under 35 U.S.C. 103 as being unpatentable over Engel et al in view of Barnes, Ashkenaz, Mendl, or Arp.

Azelastine is a phthalazinone derivative similar in structure to formulas I and II of Engel et al. Engel et al (col. 8, line 4) indicates that his compositions perform in a manner comparable to that of Azelastine. The compositions of Engel et al are antiallergic and are useful in fighting asthma, as are azelastine. The criticality of the percentages and ranges disclosed in claims 2-5 and 18 is not readily apparent to the examiner and should be supported by the submission of comparative data.

Engel et al discloses in col. 8, lines 39-42 that his composition may be applied to the skin and mucous

membranes (presumably including the eye and nose as applicant indicates in claims 1 and 12 azelastine)may be used. The medicament may be in solution.Engel et al discloses (col. 8, line 25) that the solution may be either oily or aqueous. Applicant makes similar disclosures in claims 6, 7 and 10. The solvents of claim 8 are not specifically mentioned in Engel et al. Aerosols are disclosed in col. 8, line 23 of Engel et al. Spraying is disclosed in claim 9 of applicant. Powders are disclosed in col. 8, line 23. Applicant makes similar disclosures in claims 11 and 18.

Barnes discloses droppers for dispensing solutions. Applicant discloses the use of an eye dropper as a dispenser in claim 13.

Ashkenaz discloses a pump sprayer which may be used as applicant discloses in claim 14.

Mendl discloses an atomizer which functions in a manner similar to that disclosed in claims 15 and 16.

Arp discloses a tube for dispensing ointment as disclosed in col. 17.

Claims 13-17 involve using novel compounds in known methods of dispensing. They are rendered obvious by In re Durden, 763 F.2d 1406 (Fed. Cir. 1985).

The motivation to combine Engel et al with Barnes, Ashkenaz, Mendl or Arp stems from the fact that Engel et

al discloses a medicament and Barnes, etc. disclose means of dispensing this medicament. It would therefore have been obvious to one of ordinary skill in the art of treating bronchial problems that azelastine may be dispensed in the conventional manner disclosed in claims 13-17.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Thomas et al, Vogelsang and Ehbrecht are disclosed as further examples of phthalazinones and dispensing means.

Any inquiry concerning this communication should be directed to Prater at telephone number 703-557-6525.

PSB Prater:jaw
6/15/89
6/22/89

THURMAN K. PAGE
PRIMARY EXAMINER
ART UNIT 158

TO SEPARATE, FOLD TOP AND BOTTOM EDGES, SNAP–APART AND DISCARD CARBON

FORM PTO-892 (REV. 3-78) MH
U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

NOTICE OF REFERENCES CITED

SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
07/268772	158	2

APPLICANT(S): Hettiche

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A	4769369	9/88	THOMAS ET AL.	514	234.5	
	B	4704387	11/87	ENGEL ET AL.	514	212	
	C	3813384	5/74	VOGELSANG	546	133	
	D	2995308	8/61	ASHKENAZ	239	302	
	E	2136940	11/38	EHRECHT	222	394	
	F	2457024	12/48	ARP	248	108	
	G	2119643	6/38	MENDL	222	394	
	H	1585564	1/75	BARNES	141	24	
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R

S

T

U

MP0054

EXAMINER	DATE
P. Prater	6/7/89

JC

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

430.00 1,7 CP158

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

3 DW 1-12-90

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772 Group Art Unit: 158

Filed: November 9, 1988 Examiner: P. Prater

For: AZELASTINE - CONTAINING MEDICAMENTS

December 26, 1989

* * * * *

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

The applicant respectfully requests reconsideration of the rejection of claims 1-18 in the Office Action dated June 23, 1989.

The basis of the rejection is that the Examiner considers the claimed method, composition and articles to be prima facie obvious from the disclosure of Engel et al patent 4,704,387 in view of four secondary references. Engel et al discloses compounds whose structures are similar to that of the presently claimed azelastine, differing in the R group. In the Engel patent, R is benzyl, phenethyl, methoxyethyl or allyl, whereas, in the present invention, the corresponding group is methyl. Barnes, Ashkenaz, Mendl and Arp are cited in connection with dependent claims 13-17, but are not understood to add to the relevance of Engel et al to applicant's method claims.

While the process of applicant's claims 1-12 may be prima facie obvious, that process is not obvious because it produces an unobvious result. Applicants have conducted comparative experiment which demonstrate this advantage. Regrettably, the results of these experiments have come to

hand only a few days ago, and so there has not been sufficient time to obtain a declaration. Therefore, the data is presented below. We will submit a declaration as soon as it can be obtained, after the Christmas holiday season.

The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.

The effectiveness of azelastine in preventing these symptoms in the eyes and the nose can be determined by measuring its effectiveness in preventing the liberation of histamine from sensitized rat peritoneal mast cells. The mast cells are incubated first with a test substance and then challenged with antigen. The amount of histamine released is measured, and this is compared with the total potential release of histamine. The amount of inhibition of histamine release is calculated for each test substance.

In the case of azelastine, the inhibition was 47.1% whereas, in the case of the compound of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent. This result is surprising and unexpected.

For this reason, it is submitted that the claimed process is unobvious.

In regard to claims 13-17, the Examiner cites In re Durden 763 F.2d 1406 (Fed.Cir. 1985), but that case is not thought to be relevant to the present case. In Durden, the court dealt with the obviousness of a process of making a novel compound, using a starting material which had not previously been used for that process. The process itself was

known. The court held that the process was obvious, but it cautioned against using its decision as precedent in other situations:

> We reiterate another principle followed in obviousness issue cases, which is to decide each case on the basis of its own particular fact situation. What we or our predecessors may have said in discussing different fact situations is not to be taken as having universal application.

The present case involves, in the case of claims 13-17, various forms of apparatus for dispensing azelastine into nasal or eye tissues. This is a different fact situation from the Durden case. For the reason given in the quoted passage, we submit that Durden does not deal with the patentability of this type of claim.

Furthermore, in Durden, the Court distinguished the fact situation from that in In re Kuehl, 475 F.2d 658 (C.C.P.A. 1973) where the result of the process was not foreseeable. In the present case, where there is evidence of a surprising result, it is submitted that the holding of Durden is not applicable, for the same reason as that which distinguished Durden from Kuehl.

The Kuehl case is much more relevant to the present case than Durden. The question in Kuehl was whether it was obvious to use a new zeolite in a catalytic process which had been used previously with other zeolites. The Court held that prior cases, relating to the obviousness of using a known process of making a new substance, were not relevant to that question. Further, the Court held that it was appropriate to consider the surprising result which was achieved with the new zeolite:

> We note that in the present case the novel catalyst, ZK-22, is not merely itself reduced but itself catalyzes the

hydrocarbon charge in the claimed process, a result that was not predictable until appellant had made his invention.

In the present case, the claimed articles produce a result which was not foreseeable from the teachings of the prior art, and, therefore, it is submitted that the articles of claims 13-17 are patentable.

Favorable reconsideration and allowance are respectfully requested.

The applicants have informed us that the following documents have been cited in counterparts of the present application:

German Application:

Published German Patent Application DE-OS 21 64 058, corresponding to U.S. Patent 3,813,384

Arzneimittel, Fortschritte 1972-1985, Pages 936 and 939 (1977)

Org.-Chem. drugs and their symptoms, Vol. III,m No. 6496 (1987)

European Application:

German Patent Application 3 530 793, corresponding to U.S. Patent 4,704,387.

Copies of these documents are attached.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN

By Lawrence A. Hymo

Lawrence A. Hymo

Reg. No. 19,057

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of Helmut HETTCHE

Serial No. 07/268,772

Filed: November 9, 1988

Title: AZELASTINE - CONTAINING MEDICAMENTS

Group Art Unit 158

Examiner P. Prater

Ref. No. 69931/87 217 PH
Our Account No. 03-3975
Our Order No. 326/69931

Date: December 26, 1989

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes the herewith attachment of same date and subject which is incorporated hereinto by reference and the signature below is to be treated as the signature to the attachment in the absence of a signature thereto.

Fee requirements (if any) have been calculated as shown below.

CLAIMS AS AMENDED

	Claims remaining after amendment		Highest Number previously paid for		Present Extra		Additional Fee
Total Effective Claims	18	minus	20	=	0	X $12.00 =	$ 0.00
Independent Claims	7	minus	7	=	0	X $34.00 =	$ 0.00

If amendment enters *proper* multiple dependent claim(s) into this application for *first* time, add $110.00 (per application)	$ 0.00
If *Terminal Disclaimer* enclosed, add Rule 20(d) Official fee ($56):	$ 0.00
Petition is hereby made to extend the original due date of September 23, 1989, to cover the date this response is filed for which the requisite fee is enclosed (1 month $56; 2 months $170; 3 months $390):	$ 430.00
Subtotal	$ 430.00
Less any previous extension fee *paid* since above original due date	$ 0.00
Subtotal	$ 430.00
If "small entity" verified statement filed [] previously, [] herewith, enter one-half (1/2) of subtotal and subtract	$ 0.00
TOTAL ADDITIONAL FEE ENCLOSED	$ 430.00

The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (*missing or insufficiencies only*) now or hereafter relative to this application and the resulting Official Document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof, for which purpose a *duplicate* copy of this sheet is attached. This statement does not authorize charge of the *issue* fee until/unless an issue fee transmittal sheet is filed.

1615 L Street N.W.
Washington, D.C. 20036
Tel: (202) 861-3000
Ref:

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo
Reg. No. 19,057
Sig: Lawrence A. Hymo

MP0059

orm PTO-1449 (REV. 2-83)

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use several sheets if necessary)

Sheet 1 of 1

ATTY. DOCKET NO.	SERIAL NO.
69931/88 217 PH	07/268,772
APPLICANT: Helmut HETTCHE	
FILING DATE: November 9, 1988	GROUP: 158

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
[redacted]	4,704,387	1987	Engel	514	212	
	3,813,384	1974	Vogelsang et al	546	133	

FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

PLP Org.-Chem. drugs and their synonyms, Vol. III, No. 6496 (1987)

PLP Arzneimittel, Fortschritte 1972-1985, Pages 936 and 939 (1977)

EXAMINER: P Prater

DATE CONSIDERED: 6/27/90

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

MP0060

FEB 15 1990

#4
Allen
2-15-90

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772

Filed: November 9, 1988

Group Art Unit: 158

Examiner: P Prater

For: AZELASTINE-CONTAINING MEDICAMENTS

February 12, 1990

* * * * *

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

Supplementing the response filed December 26, 1989, we enclose a declaration by Dr. Szelenyi which describes the experiments which were discussed in that response. The applicant submits that the information in the declaration supports the patentability of the claims, for the reasons given in that response.

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Telephone (202) 861-3000

Inhibition of a[illegible]rgic histamine release from ra[illegible]eritoneal mast cells

Materials and methods

Sensitization procedures and collection of peritoneal mast cells

Male Sprague-Dawley weighing between 300 and 500 g were sensitized by subcutan injection of 15 mg whole egg white (Sigma Chemical) and killed Bordetella pertussis organisms (5×10^{10}). Four weeks later, mixed peritoneal cells (3 - 5 % mast cells) were harvested in Tris-Gel buffer (composition, mM: Tris, 25; NaCl, 120; KCl, 5; and gelatin 0.01 %, pH 7.6) from peritoneal cavity of rats. The cells were centrifuged and suspended in Tris-Gel CM buffer of the following composition (mM): Tris, 25; NaCl, 120; KCl, 5; $CaCl_2$, 0.6; $MgCl_2$, 1; and 0.01 % gelatin, pH 7.6

Predetermined concentrations of whole egg white (50 µg/ml) and phosphatidyl-serine (PS, 10 µg/ml, known to enhance allergic histamine secretion) were selected to examine the influence of the drug on allergic histamine release from rat peritoneal mast cells in Tris-Gel CM buffer.

Inhibition of histamine release by drug

Reaction mixtures containing 2×10^6 peritoneal cells (3-5 % mast cells) were preincubated in presence of the drug in polypropylene tubes at 37°C for 15 min. After antigen challenge (final concentration = 50 µg/ml), the cell suspensions were incubated for an additional 30 min at 37°C and then centrifuged at 2000 rpm for 5 min at 4°C. Histamine in the supernatant was measured by the fluormetric method from Shore et al. (1959). (Kopie ist beigefügt). Histamine release, corrected for the spontaneous release, was expressed as a percentage of the total cell content. Total histamine from a separate, duplicate cell suspension was released by boiling for 10 min. Histamine release induced by whole egg white was assayed in the presence and absence of drug.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772 Group Art Unit: 158

Filed: November 9, 1988 Examiner: P. Prater

For: AZELASTINE - CONTAINING MEDICAMENTS

DECLARATION UNDER 37 CFR 1.132

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

I, Istvan Szelenyi, declare and state as follows:

1. I am a physician, and my training and experience have made me familiar with the effect of substances in treatment of the effects of allergins on nasal and eye tissues. Experiments have been conducted under my supervision to determine the effects of compounds disclosed in the above-identified application and the cited U.S. Patent 4,704,387.

2. The experiments are based on the fact that an allergic reaction in the eyes or the nose results from the liberation of histamine from mast cells as a result of the action of an antigen. The liberated histamine causes rhinitis symptoms.

3. The effectiveness of azelastine in preventing these symptoms in the eyes and the nose can be determined by measuring its effectiveness in preventing the liberation of histamine from sensitized rat peritoneal mast cells. The sensitivity of the cells is achieved through treatment with ovalbumin. The mast cells are incubated first with a test substance and then challenged with antigen. The amount of histamine released

is measured, and this is compared with the total potential release of histamine. The amount of inhibition of histamine release is calculated for each test substance. The test procedure is described in the attached Appendix A.

4. In the case of azelastine, the inhibition of liberation of histamine was 47.1% whereas, in the case of the compound of Example 1 of the cited Engel patent, the inhibition was only 24.4%.

5. Thus, azelastine was about twice as effective as the compound of Example 1 of the Engel patent.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

01/23/90 Istvan Szelenyi

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

In re PATENT APPLICATION of
Inventor(s): HETTCHE

Appln No.: 07/268,772
Series code / serial no.

Filed: November 9, 1988

Title: AZELASTINE-CONTAINING MEDICAMENTS

RECEIVED FEB 15 GROUP

Group Art Unit 158

Examiner P. Prater

Atty. Dkt. 69931 / 87 217 PH
M# / Client Ref.
(Our Deposit Account No. 03-3975)
(Our Order No. 326 / 69931
C# / M#

Date: February 12, 1990

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

15X

Sir:

SUPPLEMENTAL RESPONSE

~~RESPONSE/AMENDMENT/LETTER~~

This is a response/amendment/letter in the above-identified application and includes the herewith attachment of same date and subject which is incorporated hereinto by reference and the signature below is to be treated as the signature to the attachment in absence of a signature hereto.

* Query: Is appeal *
* deadline now? If *
* so, file Notice of *
* Appeal separately *

FEE REQUIREMENTS FOR CLAIMS AS AMENDED

	Claims remaining after amendment		Highest number previously paid for		Present Extra		Additional Fee
Total Effective Claims	* _____	minus	** _____	=	_____	X $12.00 =	$ -0-
Independent Claims	* _____	minus	*** _____	=	_____	X $36.00 =	$ _____

If amendment enters proper multiple dependent claim(s) into this application for first time - - - - - - - - - - - - - - add $120.00 + _____

Original due date: [ ] None; [ ] (date) _____

Petition is hereby made to extend the original due date to cover the date this response is filed for which the requisite fee is attached (1 month $62; 2 months $180; 3 months $430): - - - - - - - - - - - - - - - - - - + _____

If Terminal Disclaimer attached, add Rule 20(d) Official fee ($62) - - - - - - - - - - + _____

If "small entity" verified statement filed [ ] previously, [ ] herewith, enter one-half (1/2) of subtotal - - - - - - - - - - - - - - and subtract - _____

Subtotal $ -0-

Enter any previous extension fee paid since above original due date (item 4) and subtract - _____

Subtotal $ _____

TOTAL FEE ATTACHED $ -0-

2. *If the entry in this space is less than entry in the next space, the "Present Extra" result is "0".
3. **If the "Highest number previously paid for" in this space is less than 20, write "20" in this space.
4. ***If the "Highest number previously paid for" in this space is less than 3, write "3" in this space.

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficiencies only) now or hereafter relative to this application and the resulting Official Document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof, for which purpose a duplicate copy of this sheet is attached.

This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal sheet is filed.

615 L Street N.W.
Leventh Floor
Washington, D.C. 20036-5601
Tel: 861-3000
Atty/Sec: LAH/dah

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo
Sig: Lawrence A. Hymo

Reg. No. 19,057
Tel.: 861-3015

DC-120 6/89(PC) NOTE: File this cover sheet in duplicate with post card receipt (CDC-103) and attachments

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
07/268,772	11/09/88	HETTICH	H	699318721?PH

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036

EXAMINER	
PRATER, P	
ART UNIT	PAPER NUMBER
158	5

03/26/90

☐ This application has been examined ☑ Responsive to communication filed on 12/26/89 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-18 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-18 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☑ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☑ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

MP0066

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-18 are rejected under 35 U.S.C. 103 as being unpatentable over Engel et al.

The declaration supplied by the applicant, citing as unexpected the effectiveness of azelastine as compared with the preparation of Example 1 of Engel et al, is incomplete. The applicant claims several concentrations of azelastine in pharmaceutical preparations but does not indicate what concentration was used in the comparison studies. Only the terms "drug" and azelastine in general were used.

Barnes, Ashkenaz, Mendl and Arp are hereby withdrawn as references.

Applicant's arguments filed 2/12/90 have been fully considered but they are not deemed to be persuasive.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE (3) MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO (2) MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE (3) MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX (6) MONTHS FROM THE DATE OF THIS FINAL ACTION.

ELLIS P. ROBINSON
SUPERVISORY PATENT EXAMINER
ART UNIT 158

P. Prater:jaw

(703) 557-6525

03/15/90

PATENT #6

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

6-22-90

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772

Filed: November 9, 1988

Group Art Unit: 158

Examiner: P Prater

For: AZELASTINE-CONTAINING MEDICAMENTS

* * * * *

I, Istvan Szelenyi, declare and state that I am the person whose declaration was submitted on February 12, 1990 in connection with the above patent application. I further declare and state that, in the experiments described in my previous declaration, the same amounts of the respective medicines were used, i.e., azelastine and the compound disclosed in Example 1 of U.S. Patent 4,704,387. In each case, the amount used was 10 µMol/liter of mucus in the nasal cavity which was treated.

The concentration of the active component in the solution which was sprayed, in each case, was 0.01%, and 0.1 ml was sprayed in each case. In each case, the nasal cavity contained about 2.5 ml mucus. Assuming a molecular weight of about 400, it can be computed that the concentration of the active component in the nasal cavity was, as mentioned above, 10 µMol/liter.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

06/01/90 Istvan Szelenyi

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/268,772

Filed: November 9, 1988

Group Art Unit: 158

Examiner: P. Prater

For: AZELASTINE - CONTAINING MEDICAMENTS

June 18, 1990

* * * * *

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

Responsive to the Office Action of March 26, 1990, the applicant respectfully requests reconsideration.

The Examiner has based his rejection on the lack of information in the previous declaration on the amounts of medication used in the experiments reported in the declaration. A new declaration has been prepared, signed by Dr. Szelenyi who also signed the previous declaration, and that declaration is attached. In the new declaration, Dr. Szelenyi describes the amounts of medication which he used in the previous experiments. Therefore, this declaration is thought to provide the information which the Examiner indicated was needed.

A full discussion of the distinctions between the present invention and the prior art is given in the amendment dated December 26, 1989. Applicant requests that the Examiner refer to that response for the reasons why the invention overcomes the prima facie case of obviousness which the Examiner felt was established by the prior art.

Favorable reconsideration and allowance are respectfully requested.

Respectfully submitted,
CUSHMAN, DARBY & CUSHMAN

By _____
Lawrence A. Hymo
Reg. No. 19,057

1615 L Street N.W.
Washington, D.C. 20036

Telephone (202) 861-3000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

n re PATENT APPLICATION of
nventor(s): HETTCHE

ppln No.: 0 7 / 268,772
series code † † serial no.

iled: November 9, 1988

itle: AZELASTINE - CONTAINING MEDICAMENTS

Group Art Unit 158

Examiner P. Prater

Atty. Dkt. 69931 / 87 217 PH
M# / Client Ref.
(Our Deposit Account No. 03-3975)
(Our Order No. 326 / 69931
C# / M#
Date: June 18, 1990
RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCUDURE
EXAMINING GROUP 158

on. Commissioner of Patents and Trademarks
ashington, D.C. 20231

ir:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes the erewith attachment of same date and subject which is incorporated hereinto by reference and the ignature below is to be treated as the signature to the attachment in absence of a signature hereto.

FEE REQUIREMENTS FOR CLAIMS AS AMENDED

****
* Query: Is appeal *
* deadline now? If *
* so, file Notice of *
* Appeal separately *
****

	Claims remaining after amendment		Highest number previously paid for	Present Extra		Additional Fee
Total Effective Claims	* 18	minus	** 20	= 0	X $12.00 =	$ -0-
Independent Claims	* 7	minus	*** 7	= 0	X $36.00 =	$ -0-

If amendment enters proper multiple dependent claim(s) into this application for first time(leave blank if this is a reissue appln)add $120.00 + _____

Original due date: [ ] None; [X] (date) June 26, 1990

Petition is hereby made to extend the original due date to cover the date this response is filed for which the requisite fee is attached (1 month $62; 2 months $180; 3 months $430): - - - - - - - - - - - - - - - - - + _____

If Terminal Disclaimer attached, add Rule 20(d) Official fee ($62) - - - - - + _____

Subtotal $ _____

If "small entity" verified statement filed [ ] previously, [ ] herewith, enter one-half (1/2) of subtotal - - - - - - - - - - - - and subtract - _____

Subtotal $ _____

). Enter any previous extension fee paid since above original due date (item 4) and subtract - _____

L. TOTAL FEE ATTACHED $ -0-

*If the entry in this space is less than entry in the next space, the "Present Extra" result is "0".
**If the "Highest number previously paid for" in this space is less than 20, write "20" in this space.
***If the "Highest number previously paid for" in this space is less than 3, write "3" in this space.

HARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing insufficiencies only) now or hereafter relative to this application and the resulting Official Document under Rule 20, or credit any overpayment, to our count/Order Nos. shown in the heading hereof, for which purpose a duplicate copy of this sheet is attached.

his CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee ransmittal sheet is filed.

515 L Street N.W.
.eventh Floor
ashington, D.C. 20036-5601
el: 861-3000
:ty/Sec: LAH/deb

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo Reg. No. 19,057
Sig: _____ Tel.: 861-3015

OC-120 4/90(PC) NOTE: File this cover sheet in duplicate with post card receipt (CDC-103) and attachments

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
07/268,772	11/09/88	HETTCHE	6993107217PH

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036

EXAMINER	
PRATER, P	
ART UNIT	PAPER NUMBER
152	8

DATE MAILED: 06/29/90

Below is a communication from the EXAMINER in charge of this application
COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☒ THE PERIOD FOR RESPONSE:

☐ is extended to run ____________ from the date of the Final Rejection

☐ continues to run ____________ from the date of the Final Rejection

☒ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date that the shortened statutory period for response expires as set forth above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☐ Applicant's response to the final rejection, filed ____________, has been considered with the following affect, but it is not deemed to place the application in condition for allowance:

1. ☐ The proposed amendments to the claim and/or specification will not be entered and the final rejection stands because:
   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.
   b. ☐ They raise new issues that would require further consideration and/or search. (See Note).
   c. ☐ They raise the issue of new matter. (See Note).
   d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

   NOTE: ____

2. ☐ Newly proposed or amended claims ____________ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☐ Upon the filing of an appeal, the proposed amendment ☐ will be ☐ will not be, entered and the status of the claims in this application would be as follows:

   Allowed claims: ____________
   Claims objected to: ____________
   Claims rejected: ____________

   MP0074

   However;
   a. ☐ The rejection of claims ____________ on references is deemed to be overcome by applicant's response.
   b. ☐ The rejection of claims ____________ on non-reference grounds only is deemed to be overcome by applicant's response.

4. ☒ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection.

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficient reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☒ Other The combined declarations are not commensurate in scope with the claims. No basis is provided for assumption of molecular weight of 4001 Containers (Cls. 13-17) are not novel. Cls. 1 and 12 appear to be a Markush although it is not believed a Markush was intended. Cls. 2-4 do not provide acceptable ranges of physiologically active salts. Cls. 15 and 18 are indefinite.

Merrell C. Cashion

62.00 115. GP. 158

15C

MAIL ROOM JUL 12 1990 PAT. & TRADEMARK OFF. 49

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of
Inventor(s): HETTCHE, H.

(Our Deposit Account No. 03-3975
(Our Order No. 326 / 69931
C# / (Old) M#

Appln. No. 0 7 /268,772 RECEIVED
series code† †serial no.

JUL 20 1990

Group Art Unit: 158

Filed: Nov. 9, 1988

Examiner: P. Prater

Title: AZELASTINE CONTAINING MEDICAMENTS GROUP 150

Date: July 12, 1990

PETITION FOR EXTENSION OF TIME FOR COPENDENCY*

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

1. Applicant hereby petitions to extend the life of this application to and through at least the above date so as to copend with a continuing application for which extension the requisite fee is ($62 1 mo.; $180 2 mos.; $430 3 mos.; $680 4 mos.): $ 62 .00

2. If "small entity" verified statement filed [ ] herewith, [ ] previously, enter one-half (1/2) of above and ——— subtract - .00

3. Subtotal $ 62 .00

4. Enter any previous extension fee paid since last Action and ——— subtract - .00

5. CHECK ATTACHED FOR FEE OF $ 62 .00

Please charge any missing or insufficient fee re this petition to our Deposit Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached.

Respectfully submitted,

CUSHMAN, DARBY & CUSHMAN
Atty: Lawrence A. Hymo Reg. No. 19,057

By _____ Tel.: 861- 3015

Atty/Sec: LAH/dah
1615 L Street, N.W.
Eleventh Floor
Washington, D.C. 20036-5601
Tel.: 861-3000

*NOTE: This paper must be headed in the parent application of and filed in duplicate separately from Rule 60,62, continuation, division or CIP papers, with separate postcard.

100 TL 07/19/90 07268772 1 115 62.00 CK

CDC-111 4/89

PATENT APPLICATION SERIAL NO. 07 551644

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

070 LH 07/18/90 07551644 1 101 514.00 CK 62748/87-217

PTO-1556
(5/87)

MP0076

514.02, 101 A

MAIL ROOM JUL 12 1990 PAT. & TRADEMARK OFF.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

REQUEST FOR FILE WRAPPER CONTINUING APPLICATION UNDER 37 CFR 1.62 (RULE 62)

Page 1 of 4

For Design or Utility Applications

07 551644

BOX FWC

10/a

The Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior Application:
Group Art Unit: 158
Examiner: P. Prater
Atty. Dkt.: 62748 /87 217 PH
new M# / Client Ref.
(Our Deposit Account No. 03-3975
(Our Order No. 326 /62748
C# / new M#

Date: July 12, 1990

This is a RULE 62 Request for filing a

[ ] divisional

[x] continuation (any restriction/election in parent [ ] is [ ] is not carried over)

[ ] continuation-in-part without new Declaration (Rule 53(d)) [ ] without fee

[ ] continuation-in-part with new Declaration attached hereto

application under Rule 62 of prior copending parent Application No. 0 7/268,772 ,
series code† †serial no.

filed on Nov. 9, 1988 , entitled 501 AZELASTINE CONTAINING MEDICAMENTS

by the following named inventor(s) who is/are [x] the same as, [ ] less than all of (see Item 17), [ ] more than (for CIP only), those named in that parent application:

1. Inventor Helmut Hettche German
First Middle Initial Family Name Citizenship

Residence (City) Dietzenbach (State/Foreign Country) Germany DEX

Post Office Address Martinstrasse 23, D-6057 Dietzenbach

(include Zip Code) Federal Republic of Germany

2. Inventor
First Middle Initial Family Name Citizenship

Residence (City) (State/Foreign Country)

Post Office Address

(include Zip Code)

3. Inventor
First Middle Initial Family Name Citizenship

Residence (City) (State/Foreign Country)

Post Office Address

(include Zip Code)

NOTE: FOR ADDITIONAL INVENTORS, check box [ ] and attach sheet with same information for each inventor starting with inventor No. 4 and number new page 1A.

1. [ ] The Examiner's attention is directed to both the second paragraph of guideline (2) in MPEP 609 and to the last paragraph of MPEP 2001.06(b) and to the submission in the prior application of the Information Disclosure Statement and document copies filed on .

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

REQUEST FOR FILE WRAPPER CONTINUING APPLICATION UNDER 37 CFR 1.62 (RULE 62)

For Design or Utility Applications

BOX FWC

07 551644

The Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Prior Application:
Group Art Unit: 158
Examiner: P. Prater
Atty. Dkt.: 62748 /87 217 PH
new M# / Client Ref.
(Our Deposit Account No. 03-3975
(Our Order No. 326 /62748
C# / new M#

Sir:

This is a RULE 62 Request for filing a

Date: July 12, 1990

[ ] divisional

[X] continuation (any restriction/election in parent [ ] is [ ] is not carried over)

[ ] continuation-in-part without new Declaration (Rule 53(d)) [ ] without fee

[ ] continuation-in-part with new Declaration attached hereto

application under Rule 62 of prior copending parent Application No. 0 7/268,772 ,
series code† †serial no.
filed on Nov. 9, 1988 , entitled AZELASTINE CONTAINING MEDICAMENTS

by the following named inventor(s) who is/are [X] the same as, [ ] less than all of (see Item 17), [ ] more than (for CIP only), those named in that parent application:

1. Inventor Helmut Hettche German
First Middle Initial Family Name Citizenship
Residence (City)Dietzenbach (State/Foreign Country) Germany
Post Office Address Martinstrasse 23, D-6057 Dietzenbach
(include Zip Code) Federal Republic of Germany

2. Inventor
First Middle Initial Family Name Citizenship
Residence (City) (State/Foreign Country)
Post Office Address
(include Zip Code)

3. Inventor
First Middle Initial Family Name Citizenship
Residence (City) (State/Foreign Country)
Post Office Address
(include Zip Code)

NOTE: FOR ADDITIONAL INVENTORS, check box [ ] and attach sheet with same information for each inventor starting with inventor No. 4 and number new page 1A.

1. [ ] The Examiner's attention is directed to both the second paragraph of guideline (2) in MPEP 609 and to the last paragraph of MPEP 2001.06(b) and to the submission in the prior application of the Information Disclosure Statement and document copies filed on .

2. Requirement of Rule 62: The above identified prior application in which no payment of the issue fee, abandonment, or termination of proceedings occurred, is hereby expressly abandoned as of the filing date of this new application. Please use all the contents of the prior application file wrapper, including the drawings, as the basic papers for the new application. (Note: 37 CFR 1.60 (Rule 60) may be used for applications where the prior application is not to be abandoned and must be used if issue fee already paid in parent.)

3. [X] Priority is claimed under 35 U.S.C. 119/365 based on filing in Germany (country) of:

Application No.	Filing Date	Application No.	Filing Date
1. P3738681.6	Nov. 13, 1987	4.	
2.		5.	
3.		6.	

a. [ ] ____ (No.) Certified copy/copies attached.
b. [X] Certified copy/copies previously filed on Nov. 9, 1988 in prior U.S. Application No. 07/268,772 filed Nov. 9, 1988.
c. [ ] Certified copy/copies filed during International stage of PCT/___/____.
d. [ ] Priority is also claimed from PCT/___/____ filed _____.

4. [X] The prior application is assigned of record to Asta Pharma AG.

5. [ ] Attached is an Assignment to _____.

6. [X] The power of attorney in the prior application is to Cushman, Darby & Cushman, Lawrence A. Hymo, Reg. No. 19,057 (Name, Reg. No.) the address of whom is as in item 8.

7. [ ] Recognize as associate attorney _____.
(Name and Reg. No.; Address as in item 8 unless otherwise indicated)

8. Address all future communications to Cushman, Darby & Cushman, Eleventh Floor, 1615 L Street, N.W., Washington, D.C. 20036-5601.

9. Amend the specification by inserting before the first line the sentence: This is a [ ] continuation-in-part (CIP) [X] continuation [ ] division of Application No. 07/268,772, filed Nov. 9, 1988, ~~Was abandoned upon the filing hereof~~ now abandoned, which _____.

10. [ ] ____ (No.) Verified Statement(s) establishing "small entity" status under Rules 9 and 27
a. [ ] filed in above prior application (and hence applicable hereto)
b. [ ] attached.

11. Petition to extend the life of the above prior application to at least the date hereof

NOTE: One box [X] is being concurrently filed in that prior application (use Form CDC-111).
must be [ ] was previously filed in that prior application (check length of prior extension).
X'd [ ] is not necessary for copendency (double check before X'ing this box).

12. **Requirement Under Rule 62:** It is understood that secrecy under 35 U.S.C. 122 is hereby waived to the extent that if information or access is available to any one of the applications in the file wrapper of a 37 CFR 1.62 application, be it either this application or a prior application in the same file wrapper, the Patent and Trademark Office may provide similar information or access to all the other applications in the same file wrapper.

13. [ ] Please enter the amendment previously filed on _____ but unentered in the above prior application.

14. [ ] Attached: _____ sheet(s) per set of drawing of Fig(s) _____:
[ ] 1 set informal; [ ] formal of size: [ ] A4 [ ] 13" [ ] 14"

15. [ ] **PRELIMINARY AMENDMENT** to be entered before fee calculation (Do not make amendments here except cancellation of whole claims or multiple dependencies for purpose of reducing the filing fee per MPEP §§ 506 and 607; do not cancel all claims.):

16. [ ] Attached is a Rule 103(a) Petition to Suspend Action

17. Petition is hereby made requesting deletion as inventor(s) of the following who is/are not inventor(s) of the invention being claimed in this Rule 62 application:

1. _____ 2. _____

3. _____ 4. _____

18. [ ] This Rule 62 application is a continuation-in-part which discloses and claims additional matter.

a. [ ] New Declaration is attached.

b. [ ] This application is also filed under Rule 53(d) (without a Declaration) and hence filing fee is not enclosed.

FILING FEE

THE FOLLOWING FILING FEE IS BASED ON THE CLAIMS EXISTING IN THE PRIOR APPLICATION AS AMENDED AT 13 AND 15 ABOVE

19. Basic Filing Fee (enter $370.00 unless Design Appln. in which case enter $150.00) $370.00

20. Total Effective Claims 18 minus 20 = *0 x $12.00 = ---------- +-0-

21. Independent Claims 7 minus 3 = *4 x $36.00 = ---------- +144.00
*If answer is zero or less, enter "0"

22. If any proper (ignore improper) multiple dependent claim is present, add $120.00 +_____

23. Subtotal $514.00

24. If "small entity" status box 10 above is X'd, enter half (1/2) of subtotal and subtract -_____

25. TOTAL FILING FEE $514.00

26. If "assignment" box 5 above is X'd,----------add recording fee ($8.00) +_____

27. If "petition" box 16 above is X'd,----------add petition fee ($120.00) +_____

28. FEE ATTACHED $514.00

CDC-110 10/89 (1)

29. [ ] Preliminary Amendment attached (to be entered after assigning Serial No.).

30. [ ] The following PRELIMINARY AMENDMENT is to be entered after assigning Serial No.:

31. [ ] Attached:

32. **ADDITIONAL FEE CALCULATION FOR PRELIMINARY AMENDMENT PER BOXES 29/30**

		Claims remaining after amendment		Highest number previously paid for		Present Extra			Additional Fee
33.	Total Effective Claims	*	minus	**	=		x $12.00	=	$
34.	Independent Claims	*	minus	***	=		x $36.00	=	+

35. If amendment enters proper multiple dependent claim(s) into this application for first time, add $120.00 (per application) - - - - - - - - - - - - - - - - + _____

36. Subtotal $ _____

37. If "small entity" box 10 above is X'd, enter half (1/2) of subtotal - - - and subtract - _____

38. ADDITIONAL FEE $ _____

39. plus FEE from item 26 on page 3 + 514.00

40. TOTAL FEE ATTACHED $ 514.00

41. *If the entry in this space is less than entry in the next space, the "Present Extra" result is "0".

42. **If the "Highest number previously paid for" (see item 20) is less than 20, write "20" in this space.

43. ***If the "Highest number previously paid for" (see item 21) is less than 3, write "3" in this space.

44. The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed or asserted to be filed or which should have been filed herewith or with any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our deposit Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached. **This statement does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.**

1615 L Street N.W.
Eleventh Floor
Washington, D.C. 20036-5601
Tel: 861-3000
Atty/Sec: LAH/dah

CUSHMAN, DARBY & CUSHMAN
By Atty: Lawrence A. Hymo Reg. No. 19,057
Sig: _____ Tel.: 861-3015

NOTE: File this Request in duplicate with 2 post card receipts (CDC-103) & attachments if any.

CDC-110 10/89 (1)

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address : COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/551,644	07/12/90	HETTCHE	H 62748/87217P

EXAMINER: PICCONE, L

CUSHMAN, DARBY & CUSHMAN
ELEVENTH FLOOR
1615 L STREET, N.W.
WASHINGTON, DC 20036-5601

ART UNIT	PAPER NUMBER
152	11

DATE MAILED: 01/25/91

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-18 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-18 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

MP0082

EXAMINER'S ACTION

PTOL-326 (Rev.9-89)

15.

Claims 1-4, 11, 12, 15 and 18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

claim 1 use improper Markush language. Claim 1 should read....a member selected from the group.... Claims 2-4 refer to %'s of azelastine but do not indicate the applicability to the physcologically acceptable salts. Claim 12 has the same language as claim 1. The phrase "predetermined amount in claim 15 is indefinite. Claim 18 is improper and indefinite. What are conventional pharmaceutical carrier substances?

16.

Claims 11 and 18 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to those that are in the form of solutions, suspensions, oilments, creams, gels and dosage aerosols as disclosed on page 5 lines 15-16 of the specification. See M.P.E.P. §§ 706.03(n) and 706.03(z).

17.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the

date of application for patent in the United States.

18.

Claims 1, 6, 7, 9, 10, 11 and 12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vogelsang U.S. Patent 3,813,384.

Vogelsang teaches the use of substituted benzyl phthalazone derivities (column 1 line 16) as antihistamines (column 1 line 35). Azelastine is a species of the generic substituted benzyl phthalazone at column 1 line 60 when R_1 = chloro, R_2 = H P=O and y is a 7 member ring with an amine group with a methyl group as one of its substituted groups. Azelastin is the compound of Example 38 (column 10 line 30).

Vogelsang discloses the use of azelastine in a pharmaceutical preparation that can be administered in usual embodiments such as tablets, dragers, drops ointments and creams. (Column 6 line 66). Column 6 line 21 disclose the aerosol use of a substituted benzyl phthalazone derivative. Thus claims 1, 6, 7, 9, 10, 11 and 12 are met.

19.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

20.

Claims 2, 3, 4 rejected under 35 U.S.C. § 103 as being unpatentable over Vogelsang teaches Azelastine in a composition for direct administration to the nose of eye (column 1 line 57, column 6 line 65) thus meeting claims 1 and 12. Vogelsang teaches at column 7 line 2 that the recommended dosage of substituted benzyl phthalazone derivative is .4 to 4 mg per day for human patients. Claims 2, 3 and 4 would have been obvious because the proportion or amount of each ingredient is a result effective parameter dependant upon the desired medicinal effect. It would have been obvious to adjust the amount of each ingredient to optimize the effect. In the absence of new and unexpected results which differ in kind and nature it would have been obvious to vary the amount or proportion of each ingredient. The declarations submitted on February 12, 1990 and June 18, 19990 are unconvincing as to new and unexpected results in that they do not agree with the scope of the claims. All of the claims in the subject application fall within a range of from

.0005 to 2% of azelastine by weight. To be of any use the declarations must show that an amount of Azelastine at the low end, highend and mid-range, all gave unexpected results.

At column 11 line 27 Vogelsang discloses the addition of binders, preservatives, fillers etc. Claims 5, 8 and 18 would have been obvious because Vogelasng teaches the addition of other compounds to his composition so that his composition can be put into the different embodiments of pharmaceutical preparations (such as drop, ointments and creams column 6 line 69) and because no criticality is shown with respect to the ingredients mentioned in claim #8.

21.

Claims 13-17 are rejected under 35 U.S.C. § 103 as being unpatentable over Vogelsang U.S. 3,813,384 in light of Barnes U.S. 158,564, Ashkenaz U.S. 2,995,308, Mendl U.S> 119,643 and Arp U.S. 2,457,024.

Vogelsang discloses Azelastine as an antihistamine. Vogelsang does not disclose the use of an eyedropper, a pump sprayer, an atomizer or a tube for dispensing ointment. Barnes discloses droppers for dispensing solutions. Applicant discloses the use of an eye dropper as a dispenser in claim 13.

Askenaz discloses a pump sprayer which may be used as applicant discloses in claim 14.

Mendl discloses an atomizer which functions in a manner

similar to that disclosed in claims 15 and 16.

Arp discloses a tube for dispensing ointment as disclosed in col. 17.

Claims 13-17 would have been obvious because they involve dispensing a known medication in a conventional manner.

Engel, and Thomas et. al. are disclosed as further examples of phthalazinones and dispensing means. Negwer is disclosed as teaching Azelastine as a antihistamine medicament.

22.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis A. Piccone whose telephone number is (703) 308-2351.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-2351.

JRP

Piccone:ltd
January 22, 1991
(703)308-2351

THURMAN PAGE
PRIMARY EXAMINER
ART UNIT 152

TO SEPARATE, HOLD TOP AND BOTTOM EDGES, SNAP--APART AND DISCARD CARBON

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

NOTICE OF REFERENCES CITED

SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER
551 644	152	11

APPLICANT(S): Hettche

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
*	A	3 8 1 3 3 8 4	5/28/74	Vogelsang et. al.	546	133	
*	B	2 9 9 5 3 0 8	8/8/61	Ashkenez	239	302	
*	C	1 5 8 5 6 4	1/12/875	Barnes	141	24	
*	D	2 1 1 9 6 4 3	6/7/38	Mendl	222	394	
*	E	4 7 6 9 3 6 9	9/6/88	Thomas et al.	514	234.5	
*	F	4 7 0 4 3 8 7	11/3/87	Engel et. al.	514	212	
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. DWG	PERTINENT PP. SPEC.
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

*	R	Negwer, Organic-Chemicals drugs and Their Synonyms, Volume II, (1987) Page 1145
	S	
	T	
	U	

MP0088

EXAMINER	DATE
Louis A. Piccone	Dec. 19, 1990

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

IN THE UNIT) STATES PATENT AND TRADEM K OFFICE

PATENT APPLICATION

re PATENT APPLICATION of
ventor(s): HETTCHE, Helmut

pln No.: 0 7 / 551,644
eries code ↑ ↑ serial no.

led: July 12, 1990

tle: AZELASTINE-CONTAINING MEDICAMENTS

3000 117

Group Art Unit 152

Examiner L. Piccone

Atty. Dkt. 62748 / 87-217 PH
M# / Client Ref.
(Our Deposit Account No. 03-3975)
(Our Order No. 326 / 62748
C# / M#

Date: June 17, 1991

n. Commissioner of Patents and Trademarks
shington, D.C. 20231

r:

RESPONSE/AMENDMENT/LETTER

This is a response/amendment/letter in the above-identified application and includes the rewith attachment of same date and subject which is incorporated hereinto by reference and the ignature below is to be treated as the signature to the attachment in absence of a signature ereto.

FEE REQUIREMENTS FOR CLAIMS AS AMENDED

RECEIVED
JUN 24 1991
GROUP 150

1. "Small Entity" statement(s) filed	Claims remaining after amendment	Highest number previously paid for	Present Extra	Additional Fee
[ ] previously [ ] herewith((No.))				

Large/Small Entity

Total Effective Claims	* 18	minus ** 20	=		X	$20/$10 =	$
Independent Claims	* 7	minus *** 7	=		X	$60/$30 =	$
If amendment enters proper multiple dependent claim(s) into this application for first time(leave blank if this is a reissue appln)						add $200/$100	+
Original due date: [ ] None; [x] (date) April 25, 1991							
Petition is hereby made to extend the original due date to cover the date this response is filed for which the requisite fee is attached (Large/Small Entity: 1 month $100/$50; 2 months $300/$150; 3 months $730/$365):							+ 300.00
If Terminal Disclaimer attached, add Rule 20(d) Official fee ($100/$50)- - - - -							+
						Subtotal	$ 300.00
Enter any previous extension fee paid since above original due date (item 5)						and subtract	-
						TOTAL FEE ATTACHED	$ 300.00

). *If the entry in this space is less than entry in the next space, the "Present Extra" result is "0".
**If the "Highest number previously paid for" in this space is less than 20, write "20" in this space.
.***If the "Highest number previously paid for" in this space is less than 3, write "3" in this space.

HARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing insufficiencies only) now or hereafter relative to this application and the resulting Official Document under Rule 20, or credit any overpayment, to our count/Order Nos. shown in the heading hereof, for which purpose a duplicate copy of this sheet is attached.

his CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee ransmittal sheet is filed.

060 MC 06/21/91 07551644 1 117 300.00 CK
060 MC 06/21/91 07551644 1 117 270.00 CK

Query: Is appeal deadline now? If so, file Notice of Appeal separately.

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DC-120 4/91 NOTE: File this cover sheet in duplicate with post card receipt (CDC-103) and attachments

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT Application of

Helmut HETTCHE

Serial No. 07/551,644 Group Art Unit: 152

Filed: July 12, 1990 Examiner: L. Piccone

For: AZELASTINE-CONTAINING MEDICAMENTS

June 17, 1991

* * * * *

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

Responsive to the Office Action dated January 25, 1991, please amend the above-identified application as follows:

IN THE CLAIMS:

Rewrite claims 1-4 and 12 as follows:

1. (amended) A method for the treatment of irritation or disorders of the nose and eye which comprises applying directly to nasal tissues or to the conjunctival sac of the eye a medicament which contains a member [of] selected from the group consisting of azelastine and its physiologically acceptable salts.

2. (amended) A method as set forth in claim 1 in which the medicament contains 0.0005 to 2% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.0005 to 2% (weight/weight) azelastine.

3. (amended) A method as set forth in claim 2 in which the medicament contains 0.001 to 1% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.001 to 1% (weight/weight) azelastine.

4 (amended) A method as set forth in claim 1 in which the medicament contains 0.003 to 0.5% (weight/weight) of azelastine or an amount of a physiologically acceptable salt of azelastine which contains 0.003 to 0.5% (weight/weight) azelastine.

12. (amended) A method for the treatment of a patient suffering from allergy-related, or vasomotor or rhino-related colds or symptoms which comprises applying directly to the patient's nasal tissues or to the conjunctival sac of the patient's eye a medicament which contains a member [of] selected from the group consisting of azelastine and its physiologically acceptable salts.

REMARKS

The applicant respectfully requests reconsideration.

The claims have been amended in several respects to deal with the rejections under 35 U.S.C. 112. Thus, for example, the language introducing the Markush groups in claims 1 and 12 has been changed to the form suggested by the Examiner. In claims 2-4, the amounts of the physiologically acceptable salts has been described. This amendment is based on the disclosure on page 5, lines 6-8 from the bottom.

However, applicants submit that the phrase "predetermined amount" in claim 15 is not indefinite. The precise amount which is released when the atomizing container is actuated, of course, depends on two factors. First, it depends on the concentration of azelastine in the liquid in the aerosol container. Secondly, it depends on the amount of liquid which is released when the aerosol container is actuated. The two factors are selected so that the patient receives the dosage which is desired. The word

"predetermined" in this case does not imply any particular amount of liquid. Rather, it indicates that the aerosol container is one which releases a fairly precise amount each time it is actuated, so that the patient receives a desired amount.

In claim 18, it is thought that the conventional pharmaceutical carrier substances are known and need not be defined precisely. In this case, the active ingredient, azelastine, is put up in a powder. The kinds of inert components which are used to produce a pharmaceutical powder are known. While the terminology is broad, it is submitted that it is not indefinite.

Applicants respectfully traverse the rejection of claims 11 and 18 as lacking an enabling disclosure. The specification clearly teaches that it is possible to put up the claimed medicines in pharmaceutical powders. The concentration of active ingredient in the powders is disclosed at page 5, last three lines. The particle size is disclosed at page 10, lines 14-16. It is submitted that this provides sufficient information for a person skilled in the art to make the claimed compositions in the form of powders.

Applicant respectfully requests reconsideration of the rejection of claims 1, 6, 7, 9, 10, 11 and 12 as anticipated under 35 U.S.C. 102 over Vogelsang. These claims recite that azelastine is applied "directly to nasal tissues or to the conjunctival sac of the eye", and this process step is not disclosed in Vogelsang.

In discussing this ground of rejection on page 3 of the Office Action, the Examiner has not cited any portion of the reference which teaches this step. The comment that Vogelsang discloses the use of azelastine in a pharmaceutical

preparation that can be administered in usual embodiments such as tablets, etc. does not support an assertion that the reference discloses the specific form of administration claimed in this application, within the context of 35 U.S.C. 102. That provision of the patent statute is quite specific in requiring that the reference actually disclose the process which is claimed. A similar comment can be made with regard to the Examiner's contention that aerosol administration is disclosed in the reference, with the further comment that the reference does not disclose aerosol administration of azelastine (see discussion below).

The following are some of the legal authorities which define the scope of 35 U.S.C. 102.

> Ex parte Meyer, 213 USPQ 588, 590
>
> To anticipate a claimed invention, all limitations in the claims must be found in the reference since the claims measure the invention....Moreover, a rejection under 35 U.S.C. 102(e) necessarily implies that the invention is not new, i.e., that there is no difference between what is claimed and what is disclosed in the prior art. (Emphasis added.)
>
> Ex parte Stubbs, 149 USPQ 641
>
> Claims 7 and 8 are rejected as unpatentable over Jones et al. It is stated in the answer that this rejection is under 35 USC 102. However, it is apparent from the Examiner's position as to these claims that the rejection can only be under 35 U.S.C. 103 because the claims include a limitation that is not shown in the reference.
>
> In re Kalm, 154 USPQ 10
>
> A rejection under 35 U.S.C. 102(e)...necessarily implies that the invention sought to be patented has been described...that there are no differences between what is claimed and what is disclosed....

The reference simply does not disclose the step of administering azelastine "directly to nasal tissues or to the

conjunctival sac of the eye". Therefore, this ground of rejection is thought to be inappropriate.

Applicant also requests reconsideration of the rejection of the claims under 35 U.S.C. 103. Contrary to the Examiner's contention, it is submitted that Vogelsang does not disclose administering azelastine "directly to nasal tissues or to the conjunctival sac of the eye". The passages cited by the Examiner do not establish the contrary.

Column 1, line 57 discloses a category of active ingredients which include azelastine, and, as the Examiner has said, azelastine is specifically exemplified in the patent. However, this particular passage does not say anything about the mode of administration.

Column 6, line 65 which the Examiner has cited discloses various dosage forms, but, again, there is no disclosure of direct administration to nasal or eye tissues. While treatment of disorders of the skin and mucus membranes are mentioned, direct administration to nasal tissues and the conjunctival sac of the eye are not mentioned.

The Examiner has also referred to the disclosure of an aerosol, but applicant submits that the Examiner has misunderstood this disclosure. The reference does not teach putting up azelastine in an aerosol. The aerosol is used to administer histamine in a guinea-pig test. The Examiner has referred to Column 6, line 21 which is the heading for Table I. It refers to Histaminolytical activity in the histamine aerosol test on guinea-pigs. This test is described in Column 5, lines 49-63. In that test, the guinea pigs inhale an aerosol of histamine. The test compounds, such as azelastine, are administered "subcutaneously or orally" (column 5, line 58). Therefore, the disclosure of

aerosols in this reference is wholly unrelated to the use of aerosols in connection with the present invention.

The invention provides numerous advantages associated with other forms of administration. These are discussed on pages 1 and 2 of the present application. The Examiner has pointed to the declarations submitted previously, but of course these are concerned with a comparison with a different reference. These declarations show that azelastine is more effective than other active agents disclosed in the Engel reference which was cited previously. However, since the Vogelsang reference actually discloses azelastine, it raises entirely different issues.

The only routes of administration actually disclosed in Vogelsang are subcutaeous (parenteral) and oral. There is no evidence that azelastine would be effective when applied directly to nasal tissues or to the eye. The advantages of the present invention relate to a different mode of administration, but there is no suggestion of them in this reference. This is reinforced by Examples 43-46 which relate to dosage units, i.e., tablets, dragees, suppositories and injection ampoules.

Finally, applicants request reconsideration of claims 13-17. The Examiner has shown that the various appliances covered by those claims are known and that they have been used to administer medications. There can be no doubt that these appliances are not broadly new as a way to administer medications. However, it is submitted that it would not have been obvious to put up azelastine in these kinds of appliances, because it was not obvious to administer azelastine to parts of the body for which these types of appliances are suited.